## **RAW SEQUENCE LISTING**

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) no errors detected.

Application Serial Number:	10/516,780
Source:	PCT.
Date Processed by STIC:	03/29/2006

## ENTERED



PCT

**RAW SEQUENCE LISTING**PATENT APPLICATION: **US/10/516,780**DATE: 03/29/2006

TIME: 09:34:07

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

```
3 <110> APPLICANT: Allan, Bernard
       Gregoire, Francine
        Lavan, Brian
5
       Moodie, Shonna
7
        Waters, Steve
        Wong, Chi-Wai
       Metabolex, Inc.
11 <120> TITLE OF INVENTION: Methods of Diagnosing & Treating Diabetes and Insulin
12
        Resistance
14 <130> FILE REFERENCE: 016325-013600US
16 <140> CURRENT APPLICATION NUMBER: US 10/516,780
17 <141> CURRENT FILING DATE: 2004-12-03
19 <150> PRIOR APPLICATION NUMBER: US 60/386,521
20 <151> PRIOR FILING DATE: 2002-06-05
22 <150> PRIOR APPLICATION NUMBER: US 60/386,527
23 <151> PRIOR FILING DATE: 2002-06-05
25 <150> PRIOR APPLICATION NUMBER: US 60/386,551
26 <151> PRIOR FILING DATE: 2002-06-05
28 <150> PRIOR APPLICATION NUMBER: US 60/386,429
29 <151> PRIOR FILING DATE: 2002-06-06
31 <150> PRIOR APPLICATION NUMBER: US 60/386,936
32 <151> PRIOR FILING DATE: 2002-06-06
34 <150> PRIOR APPLICATION NUMBER: US 60/386,954
35 <151> PRIOR FILING DATE: 2002-06-06
37 <150> PRIOR APPLICATION NUMBER: US 60/387,301
38 <151> PRIOR FILING DATE: 2002-06-07
40 <150> PRIOR APPLICATION NUMBER: WO PCT/US03/18046
41 <151> PRIOR FILING DATE: 2003-06-05
43 <160> NUMBER OF SEQ ID NOS: 46
45 <170> SOFTWARE: PatentIn Ver. 2.1
47 <210> SEQ ID NO: 1
48 <211> LENGTH: 1909
49 <212> TYPE: DNA
50 <213> ORGANISM: Homo sapiens
52 <220> FEATURE:
53 <223> OTHER INFORMATION: human Fritz (frizzled protein homolog) cDNA
55 <220> FEATURE:
56 <221> NAME/KEY: CDS
57 <222> LOCATION: (70)..(1047)
58 <223> OTHER INFORMATION: Fritz
60 <220> FEATURE:
61 <221> NAME/KEY: modified base
62 <222> LOCATION: (42)
```

RAW SEQUENCE LISTING DATE: 03/29/2006
PATENT APPLICATION: US/10/516,780 TIME: 09:34:07

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

```
63 <223> OTHER INFORMATION: n = g, a, c or t
    65 <400> SEQUENCE: 1
W--> 66 eggagaegge ggagegggee ttgttggegt ceaetgegeg gntgeaecet geeecateet 60
     67 gccgggatca tggtctgcgg cagcccggga gggatgctgc tgctgcgggc cgggctgctt 120
     68 gecetggetg etetetgeet geteegggtg eeeggggete gggetgeage etgtgageee 180
     69 gtccgcatcc ccctgtgcaa gtccctgccc tggaacatga ctaagatgcc caaccacctg 240
     70 caccacagea etcaggacaa egecateetg gecategage agttegaagg tetgetggge 300
     71 acccactgca gccccgatct gctcttcttc ctctgtgcca tgtacgcgcc catctgcacc 360
     72 attgacttcc agcacgagcc catcaagccc tgtaagtctg tgtgcgagcg ggcccggcag 420
     73 ggctgtgagc ccatactcat caagtaccgc cactcgtggc cggagaacct ggcctgcgag 480
     74 gagetgeeag tgtacgaeag gggegtgtge ateteteeeg aggeeategt taetgeggae 540
     75 ggagctgatt ttcctatgga ttctagtaac ggaaactgta gaggggcaag cagtgaacgc 600
     76 tgtaaatgta agcctattag agctacacag aagacctatt tccggaacaa ttacaactat 660
     77 qtcattcqqq ctaaaqttaa aqaqataaaq actaaqtqcc atqatqtqac tqcaqtaqtq 720
     78 gaggtgaagg agattetaaa gteetetetg gtaaacatte caegggacae tgteaacete 780
     79 tataccagct ctggctgcct ctgccctcca cttaatgtta atgaggaata tatcatcatg 840
     80 ggctatgaag atgaggaacg ttccagatta ctcttggtgg aaggctctat agctgagaag 900
     81 tggaaggatc gactcggtaa aaaagttaag cgctgggata tgaagcttcg tcatcttgga 960
     82 ctcagtaaaa gtgattctag caatagtgat tccactcaga gtcagaagtc tggcaggaac 1020
     83 tegaaceee ggcaageaeg caactaaate eegaaataca aaaagtaaca eagtggaett 1080
     84 cctattaaga cttacttgca ttgctggact agcaaaggaa aattgcacta ttgcacatca 1140
     85 tattctattq tttactataa aaatcatqtq ataactqatt attacttctq tttctctttt 1200
     86 ggtttetget tetetettet eteaaceeet ttgtaatggt ttgggggeag actettaagt 1260
     87 atattgtgag ttttctattt cactaatcat gagaaaaact gttcttttgc aataataata 1320
     88 aattaaacat getgttaeca gageetettt getggagtet eeagatgtta atttaettte 1380
     89 tgcaccccaa ttgggaatgc aatattggat gaaaagagag gtttctggta ttcacagaaa 1440
     90 gctagatatg ccttaaaaca tactctgccg atctaattac agccttattt ttgtatgcct 1500
     91 tttgggcatt ctcctcatgc ttagaaagtt ccaaatgttt ataaaggtaa aatggcagtt 1560
     92 tgaagtcaaa tgtcacatag gcaaagcaat caagcaccag gaagtgttta tgaggaaaca 1620
     93 acacccaaga tgaattattt ttgagactgt caggaagtaa aataaatagg agcttaagaa 1680
     94 agaacatttt geetgattga gaageacaac tgaaaceagt ageegetggg gtgttaatgg 1740
     95 tagcattctt cttttggcaa tacatttgat ttgttcatga atatattaat cagcattaga 1800
     96 gaaatgaatt ataactagac atctgctgtt atcaccatag ttttgtttaa ttttgcttcct 1860
     100 <210> SEQ ID NO: 2
     101 <211> LENGTH: 325
     102 <212> TYPE: PRT
     103 <213> ORGANISM: Homo sapiens
     105 <220> FEATURE:
     106 <223> OTHER INFORMATION: human Fritz (frizzled protein homolog)
     108 <400> SEQUENCE: 2
     109 Met Val Cys Gly Ser Pro Gly Gly Met Leu Leu Arg Ala Gly Leu
     110
                          5
     112 Leu Ala Leu Ala Ala Leu Cys Leu Leu Arg Val Pro Gly Ala Arg Ala
                                         25
     115 Ala Ala Cys Glu Pro Val Arg Ile Pro Leu Cys Lys Ser Leu Pro Trp
    116
                 35
                                     40
     118 Asn Met Thr Lys Met Pro Asn His Leu His His Ser Thr Gln Asp Asn
     119
                                 55
```

RAW SEQUENCE LISTING DATE: 03/29/2006
PATENT APPLICATION: US/10/516,780 TIME: 09:34:07

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

121 Ala Ile Leu Ala Ile Glu Gln Phe Glu Gly Leu Leu Gly Thr His Cys 70 124 Ser Pro Asp Leu Leu Phe Phe Leu Cys Ala Met Tyr Ala Pro Ile Cys 125 85 127 Thr Ile Asp Phe Gln His Glu Pro Ile Lys Pro Cys Lys Ser Val Cys 128 105 130 Glu Arg Ala Arg Gln Gly Cys Glu Pro Ile Leu Ile Lys Tyr Arg His 115 120 133 Ser Trp Pro Glu Asn Leu Ala Cys Glu Glu Leu Pro Val Tyr Asp Arg 135 136 Gly Val Cys Ile Ser Pro Glu Ala Ile Val Thr Ala Asp Gly Ala Asp 137 145 150 155 139 Phe Pro Met Asp Ser Ser Asn Gly Asn Cys Arg Gly Ala Ser Ser Glu 165 142 Arg Cys Lys Cys Lys Pro Ile Arg Ala Thr Gln Lys Thr Tyr Phe Arg 180 185 145 Asn Asn Tyr Asn Tyr Val Ile Arq Ala Lys Val Lys Glu Ile Lys Thr 195 200 148 Lys Cys His Asp Val Thr Ala Val Val Glu Val Lys Glu Ile Leu Lys 215 220 151 Ser Ser Leu Val Asn Ile Pro Arg Asp Thr Val Asn Leu Tyr Thr Ser 230 235 154 Ser Gly Cys Leu Cys Pro Pro Leu Asn Val Asn Glu Glu Tyr Ile Ile 245 250 157 Met Gly Tyr Glu Asp Glu Glu Arg Ser Arg Leu Leu Val Glu Gly 260 265 160 Ser Ile Ala Glu Lys Trp Lys Asp Arg Leu Gly Lys Lys Val Lys Arg 161 275 280 163 Trp Asp Met Lys Leu Arg His Leu Gly Leu Ser Lys Ser Asp Ser Ser 295 166 Asn Ser Asp Ser Thr Gln Ser Gln Lys Ser Gly Arg Asn Ser Asn Pro 167 305 310 315 169 Arg Gln Ala Arg Asn 170 325 173 <210> SEQ ID NO: 3 174 <211> LENGTH: 2540 175 <212> TYPE: DNA 176 <213> ORGANISM: Mus musculus 178 <220> FEATURE: 179 <223> OTHER INFORMATION: mouse Fritz (frizzled-related protein) cDNA 181 <220> FEATURE: 182 <221> NAME/KEY: CDS 183 <222> LOCATION: (365)..(1336) 184 <223> OTHER INFORMATION: Fritz 186 <220> FEATURE: 187 <221> NAME/KEY: modified base 188 <222> LOCATION: (1)..(2540) 189 <223> OTHER INFORMATION: n = g, a, c or t 191 <400> SEQUENCE: 3

**RAW SEQUENCE LISTING**PATENT APPLICATION: **US/10/516,780**DATE: 03/29/2006

TIME: 09:34:07

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

```
192 gaatteggea egagetgaat ttgacttttg tttttattte tetetggett cetettetge 60
     193 cccctcatct gattgatgtg ctaaggctga tgtctctgcc agagcgagag gaataaatag 120
     194 atgctgcctc gcctagaggc ttagacgctt gggaagagca gccggcgcac gagcgaccgg 180
     195 geteegeeaa getagtggae eggaeetggg ageaettgga tecaagagaa etgtgattgt 240
     196 cccaggggtg ggggcagete cccaggtegt tgggateace ceteggaace gcagggggag 300
     197 actteggaac gaaagtgtet eeegegteeg tegetegtge geeetgeece ateetgetgg 360
     198 gaccatggtc tgctgcggcc cgggacggat gctgctagga tgggccgggt tgctagtcct 420
     199 ggctgctctc tgcctgctcc aggtgcccgg agctcaggct gcagcctgtg agcctgtccg 480
     200 catecegetg tgeaagteee tteeetggaa catgaceaag atgeeeaace acetgeacea 540
     201 cagcacccag gctaacgcca tcctggccat ggaacagttc gaagggctgc tgggcaccca 600
     202 ctgcageceg gatettetet tetteetetg tgcaatgtae geacecattt geaceatega 660
     203 cttccagcac gagcccatca agccctgcaa gtctgtgtgt gagcgcgccc gacagggctg 720
     204 cgagcccatt ctcatcaagt accgccactc gtggccggaa agcttggcct gcgacgagct 780
     205 gccqqtqtac qaccqcqqcq tqtqcatctc tcctqaqqcc atcqtcaccq cqqacqqaqc 840
     206 ggattttcct atggattcaa gtactggaca ctgcagaggg gcaagcagcg aacgttgcaa 900
     207 atgtaageet gteagageta cacagaagae etattteegg aacaattaca actatgteat 960
     208 ccgggctaaa gttaaagagg taaagatgaa atgtcatgat gtgaccgccg ttgtggaagt 1020
     209 qaaqqaaatt ctaaaqqcat cactqqtaaa cattccaaqq qacaccqtca atctttatac 1080
     210 cacctotggc tgcctctgtc ctccacttac tgtcaatgag gaatatgtca tcatgggcta 1140
     211 tgaagacgag gaacgttcca ggttactctt ggtagaaggc tctatagctg agaagtggaa 1200
     212 ggatcggctt ggtaagaaag tcaagcgctg ggatatgaaa ctccgacacc ttggactggg 1260
     213 taaaactgat gctagcgatt ccactcagaa tcagaagtct ggcaggaact ctaatccccg 1320
     214 gccagcacgc agctaaatcc tgaaatgtaa aaggccacac ccacggactc ccttctaaga 1380
     215 ctggcgctgc tggactaaca aaggaaaacg cacagttgtg ctcgtgaccg attgtttacc 1440
     216 gcagacaccg cgtggctacc gaagttactt ccggtcccct ttctcctgct tcttaatggc 1500
     217 ctggggttag atcctttaat atgttatata ttctgtttca tcaatcacgt ggggactgtt 1560
     218 cttttgcaac cagaatagta aattaaatat gttgatgcta aggtttctgt actggactcc 1620
     219 ctgggtttaa tttggtgttc tgtaccctga ttgagaatgc aatgtttcat gtaaagagag 1680
     220 aatcctggtc atatctcaag aactagatat tgctgtaaga cagcctctgc tgctgcgctt 1740
     221 atagtettgt gtttgtacet gtttggecat tteeeteatg etgtgaaagt tatacatgtt 1800
     222 tataaaggta gaacggcatt ttgaaatcag acactgcaca agcagagtag cccaacacca 1860
     223 ggaagcattt atgaggaaac gccacacagc atgacttatt ttcaagattg gcaggcagca 1920
     224 aaataaatag tgttgggagc caagaaaaga atattttgcc tggttaaggg gcacactgga 1980
     225 atcagtagec ttgagecatt aacagcagtg ttettetgge acgtttttga tttgtteata 2040
     226 aatgtattca cgagcattag agatgaactt ataactagac atctgttgtt atcactatag 2100
     227 ctctgcttcc ttctaaatca aacccattgt tggatgctcc ctctccattc ataaataaat 2160
     228 ttqqcttqct qqtattqqcc aqqaaaaqaa aqtattaaaq tatqcatqca tqtqcaccaq 2220
     229 qqtqttattt aacaqaqqta tqtaactcta taaaaqacta taatttacaq qacacqqaaa 2280
     230 tgtgcacatt tgtttacttt ttttcttcct tttgctttgg gcttgtgatt ttggtttttg 2340
W--> 231 gtgtgtttat gtctgtattt tggggggtgg gtaggtttaa nccattgcac attcaagttg 2400
W--> 232 nactagatta gagtagacta ggctcattgg cctagacatt atgatttgaa tttgtgttgt 2460
     233 ttaatgctcc atcaagatgt ctaataaaag gaatatggtt gtcaacagag acgacaacac 2520
                                                                           2540
     234 ccaaaaaaaa aaaaaaaaaa
     237 <210> SEQ ID NO: 4
     238 <211> LENGTH: 323
     239 <212> TYPE: PRT
     240 <213> ORGANISM: Mus musculus
     242 <220> FEATURE:
     243 <223> OTHER INFORMATION: mouse Fritz (frizzled-related protein)
```

RAW SEQUENCE LISTING DATE: 03/29/2006
PATENT APPLICATION: US/10/516,780 TIME: 09:34:07

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

245 <400> SEQUENCE: 4 246 Met Val Cys Cys Gly Pro Gly Arg Met Leu Leu Gly Trp Ala Gly Leu 249 Leu Val Leu Ala Ala Leu Cys Leu Leu Gln Val Pro Gly Ala Gln Ala 2.0 25 252 Ala Ala Cys Glu Pro Val Arg Ile Pro Leu Cys Lys Ser Leu Pro Trp 255 Asn Met Thr Lys Met Pro Asn His Leu His His Ser Thr Gln Ala Asn 55 258 Ala Ile Leu Ala Met Glu Gln Phe Glu Gly Leu Leu Gly Thr His Cys 261 Ser Pro Asp Leu Leu Phe Phe Leu Cys Ala Met Tyr Ala Pro Ile Cys 85 90 264 Thr Ile Asp Phe Gln His Glu Pro Ile Lys Pro Cys Lys Ser Val Cys 267 Glu Arg Ala Arg Gln Gly Cys Glu Pro Ile Leu Ile Lys Tyr Arg His 115 120 270 Ser Trp Pro Glu Ser Leu Ala Cys Asp Glu Leu Pro Val Tyr Asp Arg 135 273 Gly Val Cys Ile Ser Pro Glu Ala Ile Val Thr Ala Asp Gly Ala Asp 150 155 276 Phe Pro Met Asp Ser Ser Thr Gly His Cys Arg Gly Ala Ser Ser Glu 165 170 279 Arg Cys Lys Cys Lys Pro Val Arg Ala Thr Gln Lys Thr Tyr Phe Arg 180 185 282 Asn Asn Tyr Asn Tyr Val Ile Arg Ala Lys Val Lys Glu Val Lys Met 195 200 285 Lys Cys His Asp Val Thr Ala Val Val Glu Val Lys Glu Ile Leu Lys 210 215 220 288 Ala Ser Leu Val Asn Ile Pro Arg Asp Thr Val Asn Leu Tyr Thr Thr 230 235 291 Ser Gly Cys Leu Cys Pro Pro Leu Thr Val Asn Glu Glu Tyr Val Ile 245 250 294 Met Gly Tyr Glu Asp Glu Glu Arg Ser Arg Leu Leu Val Glu Gly 265 297 Ser Ile Ala Glu Lys Trp Lys Asp Arg Leu Gly Lys Lys Val Lys Arg 280 300 Trp Asp Met Lys Leu Arg His Leu Gly Leu Gly Lys Thr Asp Ala Ser 295 300 303 Asp Ser Thr Gln Asn Gln Lys Ser Gly Arg Asn Ser Asn Pro Arg Pro 304 305 310 315 306 Ala Arq Ser 309 <210> SEQ ID NO: 5 310 <211> LENGTH: 1740 311 <212> TYPE: DNA 312 <213> ORGANISM: Homo sapiens 314 <220> FEATURE: 315 <223> OTHER INFORMATION: human p21 activated kinase 1B (PAK1B) cDNA 317 <220> FEATURE:

RAW SEQUENCE LISTING ERROR SUMMARY DATE: 03/29/2006 PATENT APPLICATION: US/10/516,780 TIME: 09:34:08

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

## Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of/each sequence which presents at least one n or Xaa.

Seq#:1; N Pos. 42 / Seq#:3; N Pos. 2381,2401 VERIFICATION SUMMARY

PATENT APPLICATION: US/10/516,780

DATE: 03/29/2006 TIME: 09:34:08

Input Set : A:\-136.APP

Output Set: N:\CRF4\03292006\J516780.raw

L:66 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0 L:231 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:2340 L:232 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:3 after pos.:2400